REMARKS

Claims 7-23 are active in the present application.

The rejections of Claims 7, 8, 10, and 11 under 35 U.S.C. §102(b) and under 35 U.S.C. §103(a) over McQuillen et al are obviated in part by amendment and traversed in part.

The claimed *E. coli* strains claimed in Claims 7, 8, 10-11, and 23 are not the same as the McQuillen et al *E. coli* for the reasons of record, which are further explained hereinbelow.

The present invention provides, in part, an isolated *Escherichia coli*, which has an ability to produce and accumulate arginine in a medium when the bacterium is cultivated in the medium, and which is *modified to have an enhanced ability to utilize acetate*, whereby the ability to produce arginine is enhanced compared to the unmodified bacterium (see Claim 7).

McQuillen et al discloses *E. coli* strain B, which is a wild type strain (see page 81, "Methods", line 1). However, McQuillen et al do not disclose or suggest making a mutant *E. coli* strain or modify a wild-type *E. coli* so that it may utilize acetate as in Claim 7.

Applicants point out that a wild type *E. coli* are unable to utilize acetic acid or acetate as the sole carbon source or which has been modified to utilize acetate. Applicants direct the Examiner's attention to *E. coli* strain 237 noted in the specification on page 8, line 14-19, which was unable to utilize acetic acid or acetate as a sole carbon source on an agar medium to grow or form colonies within two days at 37°C (see page 9, lines 1-6). In contrast, a mutant strain, which was modified to have an ability to utilize acetate (e.g., strain 382), does have this ability. Therefore, the disclosure of McQuillen et al fails to anticipate the presently claimed invention.

In this respect, the Examiner notes that the argument presented on April 22, 2003 is drawn to "a mutant strain", which was not a limitation of the claim. In order to appease the

Examiner, Applicants have amended Claims 7 and 8 to specifically recite that the strain of *Escherichia coli* is, in fact, a mutant strain of *Escherichia coli*. Therefore, the claims and the data shown in Tables 2 and 3 are commensurate in scope.

Furthermore, the Examiner asserts: "The burden is on Applicant to show that the reference microorganism does not absolutely produce arginine in a medium containing acetic acid or acetate as the lone source. The instant specification only indicates that the strain on page 8 grows poorly but there is absolutely no indication that no arginine was produced." (page 6, lines 5-9 of paper number 11). However, present claim 7 recites, in part: "whereby the ability to produce arginine is *enhanced compared* to the unmodified bacterium." Accordingly, the present invention is clearly distinct from McQuillen et al, which is analogous to what the Examiner even admits is poor growth and must not be sufficient to meet the "enhanced" abilities of arginine by the claimed bacterium.

The Examiner cites *In re Brown* and *In re Best* to support the premise that when a reference reasonably teaches a product that is identical or substantially identical or are produced by identical or substantially identical process, the PTO may require the Applicant to prove that the prior art products do not inherently possess the characteristics of the claimed product. In so doing, the Examiner states that the burden is shifted to the Applicant to prove that the reference product is not within the scope of the claimed invention. However, Applicants note that the Examiner has not even remotely met the burden necessary to shift the burden to the Applicant. Certainly the Examiner must provide a better basis to support the conclusion that the bacterium of McQuillen et al is identical or substantially identical to the claimed bacterium. Applicants can find no support in the MPEP or in case law that supports the notion that a mere conclusory statement by an Examiner without any support to justify

that conclusion would support the "reasonably teaches" threshold. In fact, this position by the Examiner is in direct odds with case precedent.

The Examiner's attention is drawn to *Ex parte* Jones, 62 USPQ2d 1206, 1208 (Bd. Pat. App. & Inter. 2001) (**copy enclosed**), which states that: when an Examiner maintains that there is an implicit teaching or suggestion in the prior art, "the Examiner should indicate where (page and line or figure) such a teaching or suggestion appears in the prior art." The Board has also stated that the burden of proving inherency lies on the Examiner, stating: "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." (*Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990); **copy enclosed**). Accordingly, Applicants submit that the Examiner has not successfully shifted the burden to the Applicant to prove that the strain of McQuillen et al does not fall within the scope of the present claims.

Even if the Examiner had met his burden, Applicants submit that the clear distinction between the inventive bacterium and that disclosed by McQuillen et al as highlighted above would clearly distinguish the present invention from this disclosure. In addition, Applicants have shown adequate data to support a distinction between the presently claimed invention and the disclosure of McQuillen et al, especially in view of the fact that claims in question are specifically drawn to a mutant strain of *E. coli*.

Moreover, the growth medium used to culture the *E. coli* strain in McQuillen et al contained significant amounts of glucose as the carbon source (see page 82, line 1), which is different from those bacteria claimed in, for example, Claims 8 and 9, which recite that the *E. coli* can grow on an agar medium using acetic acid or acetate as a sole carbon source.

The Examiner's attention is drawn to Table 2 on page 11 and Table 3 on page 12, which are reproduced below for the Examiner's convenience:

Table 2

Strain	Arginine (g/L)
237 (parent)	5.1
382 (acetate utilizing mutant)	12.0
383 (acetate utilizing mutant)	7.7

Table 3

Strain	Arginine (g/L)	Yield from glucose (%)
237 (parent)	4.5	5.2
382 (acetate utilizing mutant)	19.3	23.9

As these data clearly show, when the claimed acetate utilizing mutant *E. coli* is directly compared to the strain corresponding to McQuillen et al, the claimed bacterium is clearly distinct. Applicants once again note that the Examiner appears to have missed the clear difference in production of L-arginine in the strains of the present invention (i.e., strain 382) and the strain corresponding to McQuillen et al (i.e., strain 237). This clear difference, on its own, is sufficient to demonstrate that McQuillen et al cannot anticipate the claimed invention.

Moreover, Applicants draw the Examiner's attention to Table 1 (page 10), which corresponds to the experiment set forth in Example 2 and was performed in an acetate environment. For the Examiner's convenience, Table 1 is reproduced below:

Table 1

Strain	Growth (OD540) in liquid minimal medium For 16 hours with:	
	Glucose (0.5%)	Ammonia acetate (0.5%)
237 (parent)	1.8	0.4
382	1.5	1.0
383	1.6	0.7

As is clearly evident above, the wild type 237 strain was unable to utilize acetate as the sole carbon source in producing L-arginine to nearly the same efficiency compared to bacterial strains, which had been modified to utilize acetate as the sole carbon source (strain 382). Again, based on this showing it is clear that the present invention is distinct from that of McQuillen et al, and therefore this reference cannot anticipate the claimed invention.

Moreover, citing In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974), MPEP §2143.03 states: "To establish a prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." Applicants submit that based on the failure of McQuillen et al to disclose or suggest the presently claimed bacterium, the disclosure of McQuillen et al fails to meet this requirement.

Applicants further note that:

> Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). See also *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The courts have also held that:

> The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)

In the present application, the artisan would have no reasonable expectation of the advantageous properties flowing from the inventive bacterium based on the disclosure of McQuillen et al, nor would the artisan envision the mutant *E. coli* strain that possesses an enhance acetate utilizing property. Accordingly, there cannot be a reasonable basis for the Office to maintain that the present invention as claimed in Claims 7, 8, 10, and 11 would even be obvious in view of McQuillen et al.

Therefore, for all the foregoing reasons, Applicants submit that the present invention is not anticipated by or obvious in view of McQuillen et al.

Withdrawal of these grounds of rejection is requested.

The rejection of Claims 7-8, 10-11, and 23 under 35 U.S.C. §112, first paragraph (written description), is traversed.

As stated in the Amendment and Request for Reconsideration, filed on July 18, 2002, and reiterated on April 22, 2003:

> As this rejection may apply to the present claims, Applicants note that deposit receipts for the deposited strains FERM BP-7925 and FERM BP-7926 were filed on June 22, 2001. These strains are specifically identified on page 8, lines 14-19 and page 9, lines 11-16. As noted on those pages, those strands have been deposited under the terms of the Budapest Treaty. In accordance with such deposit, Applicants submit that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

At page 4, lines 16-19 of paper number 18, the Examiner has required the addition of the identifying information set forth in 37 C.F.R. §1.809(d) to the specification. 37 C.F.R. §1.809(d) requires inclusion of the following information:

(1) The accession number for the deposit;
(2) The date of the deposit;
(3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and
(4) The name and address of the depository.

Applicants submit that no further amendment is necessary, since this information is already in the specification.

Specifically, Applicants point to page 5, 11-18, which provides the depository, date of deposit, and the accession number. In addition, Applicants point to Example 1 (page 8, line 4 to page 9, line 16), which fully describes characteristics of the deposited mutant *E. coli* cell strains. In particular, these strains have an ability to produce and accumulate arginine in a medium when the bacterium is cultivated in the medium, and which is modified to have an enhanced ability to utilize acetate, whereby the ability to produce arginine is enhanced compared to the unmodified bacterium. Moreover, this information has been added to Claim 7. Therefore, Applicants submit that the present claims are drawn to a deposited material, as such the Examiner would be able to compare the presently claimed invention to any prior art. In fact, the Examiner has already compared the present invention to the prior art (i.e., McQuillen et al).

The Examiner has taken the position that "One of the basic issues which has not been addressed and supplied by Applicant is the requirement as noted by number (3) of page 5 of the remarks: "A description of the deposited biological material sufficient to specifically identify it and to permit examination" (paper number 18, page 2, line 31 to page 3, line 3). Specifically, the Examiner has taken the position that the specification must provide: (a) the

morphological characteristics of the claimed cell strain in various growth mediums and comparisons to the parent strain with respect to shape and size dimensions; (b) the mode of proliferation; and (c) physiological characteristics pertaining to fermentation and assimilation and a comparison to the parent strain (paper number 18, page 3, line 10-18).

Applicants note that the U.S. Courts have long held that availability of a biological product via a public depository provides an acceptable means of meeting the written description and the enablement requirements of 35 U.S.C. §112, first paragraph (see *In re Argoudelis*, 434 F.2d 1390, 1392, 168 USPQ 99, 102 (CCPA 1970)). The Examiner acknowledges full agreement with the courts in *In re Argoudelis*; however, attempts to distinguish the present application from *In re Argoudelis*. The Examiner notes that the present application may be distinguished from *In re Argoudelis*, stating:

> As for the microorganisms, there is a description requirement which the instant specification lacks that was met by the above decision, see page 4 which states "**A detailed taxonomic description of the microorganism was also disclosed.**" (emphasis in original; paper number 18, page 4, lines 11-14)

Further, the Examiner exhorts that "Applicant may have to go to the Board of Appeals to obtain any allowable claims absent the **taxonomic description of the microorganisms**." (emphasis in original; paper number 18, page 5, lines 23-24).

In the present application, as well as the claims, Applicants do *in fact* provide the requisite taxonomic description as the claims absolutely recite that the claimed microorganism is "A mutant strain of *Escherichia coli*".

The following sources may be noted for the following definition of "taxonomy":

a) 1) The study of the general principles of scientific classification; 2) orderly classification of plants and animals according to their presumed natural relationship (Merriam Webster's Collegiate Dictionary, 10th Edition, 1994)

b) The classification (arrangement), nomenclature (naming), and identification of organisms (Microbiology: Concepts and Applications; Pelczar MJ, et al, 1993)

c) The classification of various living things or organisms, divided into groups to show degrees of similarity or presumed evolutionary relationship (Webster's New World/Stedman's Concise Medical Dictionary, 1987)

In view of the foregoing, even the layperson would appreciate that the present claims provide a taxonomic description: genus – *Escherichia*, species – *coli*. Moreover, the skilled artisan would immediately envision the morphological characteristics for identifying *E. coli*, as this is one of the central tenants of taxonomic classification. Further, Applicants note that the characteristics for identifying a mutant strain of *E. coli* of the present invention are described, for example, in Example 1 of the specification. Therefore, the description provided in the specification augmented by the knowledge generally available to the skilled artisan would readily place the claimed invention in the hands of the artisan and clearly convey that the Applicant was in possession of the full scope of the invention at the time of invention thereof.

Therefore, since the Examiner "fully agrees" with the *In re Argoudelis* decision and Applicants have provided the requisite taxonomic description, which the Examiner had deemed as being the difference between the present application and the application of Argoudelis, Applicants submit that this rejection is not tenable.

Applicants further note that the Examiner attempts to bolster his rejection by citing *In re Hammack*, *In re Venezia*, *In re Goffe*, *In re Watson*, *In re Knowlton*, *In re Steele*, *In re Moore*, and *In re Merat*. (**copies enclosed**) However, as is clearly evident, none of these cases pertain to biotechnology and the special problems in this art relating to 35 U.S.C. §112, first paragraph. Therefore, the proper precedent for establishing the adequacy of the claimed microorganism under 35 U.S.C. §112, first paragraph, is that of *In re Argoudelis* and not

those enunciated by *In re Hammack*, *In re Venezia*, *In re Goffe*, *In re Watson*, *In re Knowlton*, *In re Steele*, *In re Moore*, and *In re Merat*. The Examiner has already conceded the holding of *In re Argoudelis* that availability of a biological product via a public depository provides an acceptable means of meeting the written description and the enablement requirements of 35 U.S.C. §112, first paragraph. Therefore, Applicants submit that the deposit of the claimed microorganisms satisfies the *In re Argoudelis* standard for examining biotechnology applications.

Accordingly, Applicants submit that this ground of rejection by the Examiner is not tenable and request that it be withdrawn.

With respect to the non-elected claims drawn to methods of producing arginine (Group III, see Claims 15-22), Applicants request that upon finding that the elected group is found to be allowable (Claims 7-14), the corresponding non-elected process claims should be rejoined in accordance with MPEP §821.04.

Applicants submit that the application is now in condition for allowance, and early notification of such action is earnestly solicited.

Respectfully submitted,

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